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EXAMINER	
GAMBEL, PHILLIP	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,109	TEDESCO ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/06/2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37,39-44,46 and 48-88* is/are pending in the application.

4a) Of the above claim(s) *50-55, 57, 59-71 and 73-76* is/are withdrawn from consideration.

5)☒ Claim(s) *72* is/are allowed.

6)☒ Claim(s) *37,39,40,49,56,58,72 and 80-88* is/are rejected.

7)☒ Claim(s) *41-44,46,48 and 77-79* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/06/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 10/06/2010, has been entered.

Claims 37, 44, 49 and 72 have been amended.

Claim 88 has been added.

Claim 45 has been canceled.
Claims 1-36, 38 and 47 have been canceled previously.

Claims 37, 39-44, 46 and 48-88 are pending.

Claims 37, 39-44, 46, 48-49, 56, 58, 72 and 77-88 are under consideration as they read on the elected invention.

Claims 50-55, 57, 59-71 and 73-76 have been withdrawn as they read on non-elected inventions.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Action will be in response to applicant's amendment, filed 10/06/2010.

The rejections of record can be found in previous Office Action, mailed 07/07/2010.

3. Applicant's submission, filed 10/06/2010, has placed this application in compliance with the Sequence Rules.

4. The substitute specification in compliance with applicant's statements filed, 10/06/2010, has been entered and is in compliance with 37 CFR 1.125(b).

5. Upon reconsideration of applicant's amended claims, filed 10/06/2010, the previous rejection under 35 U.S.C. § 112, second paragraph, has been withdrawn.

6. Upon reconsideration of applicant's amended claims and arguments, filed 10/06/2010, the previous rejection under 35 U.S.C. § 112, first paragraph, has been withdrawn in view that the claimed antibodies must bind SEQ ID NO: 15 and inhibit the conversion of C5 alpha chain to C5a and C5b, including the reliance of such specificity to various mammalian species exemplified in Example 9.

7. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 49 and 82-87 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Antibodies are glycoproteins that possess the ability to react in vitro and in vivo specifically and selectively with the antigenic determinants or epitopes eliciting their production or with an antigenic determinant closely related to the homologous antigen.
Antibodies are immunoglobulins that are formed in response to immunogens or that are screened for specificity an antigen / immunogen.

It has been well established in the art that the antigen binding specificity is critical to how the skilled artisan would employ antibodies in various modalities (e.g., affinity purification, detection or diagnostic assays, bioassays, treatment), including those consistent with the instant disclosure (see specification, including the Summary and Detailed Description of the Invention).

However, the instant claims, particularly independent claim 49 do not recite an antigen specificity for C5 alpha chain and more particularly for SEQ ID NO: 15, including the ability to inhibit the conversion of 5 alpha chain to C5a and C5b.

The specification provides insufficient direction or guidance regarding how to use antibodies or immunoglobulin chains or chimeric proteins comprising the claimed sequences in the absence of an antigen specificity for human C5a and yet retain substantially the same binding specificity of the claimed chimeric proteins / antibodies, which are enabling consistent with the disclosed utilities of the instant disclosure (see Summary and Detailed Description of the Invention of the instant specification).

Given the well known polymorphism of antibodies, it would have been undue experimentation to make and use the vast repertoire of antibodies and immunoglobulin chains encompassed by the claimed invention in the absence of binding specificity for C5a to enable the scope of the claimed antibodies encompassed by the claimed invention.

Without sufficient guidance and given the well known complexity and unpredictability of using antibodies and immunoglobulin chains with no particular antigen specificity as well the well known polymorphism of antibodies; it would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue to make and use the vast repertoire of antibodies broadly encompassed by the claimed invention in order to make and use the anti-C5a antibodies / chimeric proteins consistent with the instant disclosure.

Applicant is invited to amend the claims to recite the appropriate antigen specificity to obviate this rejection.

9. Claims 37, 39-40, 56, 58, 72, 80-83 and 85-88 are rejected under 35 U.S.C. § 102(b) as being anticipated or in the alternative are rejected under 35 U.S.C. § 103(a) as being unpatentable by Evans et al. (U.S. Patent 6,355,245) (see entire document) essentially for the reasons of record.

Applicant's arguments, filed 10/06/2010, have been fully considered but have not been found convincing essentially for the reasons of record.

Evans et al. contains a general teaching that one can raise an antibody against C5 and a specific teaching of one such antibody (5Gl.1). Neither teaching anticipates the claimed invention. In regards to the general teaching that one can raise Abs against C5, Applicants claim here a specific antibody that recognizes and binds a region corresponding to sequence 727-744 (SEQ ID NO:15) of the C5 component of human complement, which results in an inhibition of the conversion of the C5 alpha chain to C5a and C5b. That antibody is not disclosed in and therefore not anticipated by the general teaching of Evans et al. In regards to the specific 5Gl.1 antibody, the Examiner seems to have taken the position that that Ab may inherently anticipate the claimed invention. However, as shown in Example 13 of Evans et al., the 5Gl.1 antibody does not bind to the peptides corresponding to the C5a cleavage site.

Although Evans et al. teach human antibodies that prevent cleavage of C5 to form C5a and C5b, the disclosure does not contain each and every element as set forth in the presently rejected claims. Specifically, Evans et al. do not expressly teach an antibody that "recognizes a region corresponding to sequence 727-744 (SEQ ID NO: 15) of the C5 component of human complement or a region having at least 80% homology thereto." The Examiner also acknowledged that Evans et al "does not explicitly teach the amino acid residues 731-740 of C5." (OA at p. 8.) The Examiner stated that "it is Applicant's burden to show that the reference antibody [5Gl.1] does not bind or cross-react with the same cleavage site or epitope." (OA at p. 8.). However, Evans et al. themselves provide the requested showing in Example 13 of the patent. Their attempts to characterize an epitope recognized by the referenced antibody yielded negative results, with the only conclusion being that "peptides corresponding to the C5a cleavage site did not bind to the 5Gl.1 antibody." (Col. 53, 11. 14-15). Therefore, the disclosure of Evans et al. does not expressly anticipate the claimed invention.

Nor does it provide an inherent disclosure of the claimed antibody. Under Robertson v. Scripps, the disclosure of Evans et al. does not inherently anticipate the claimed invention, because it does not establish that the missing requirement of Ab binding to the specific SEQ ID is necessarily a characteristic of the reference Ab (as evidenced in Example 13). In addition, Evans et al. do not enable the claimed antibody. Anticipation requires a prior art reference to be enabling such that the claimed subject matter may be made or used by one skilled in the art. Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1354 (Fed. Cir. 2003). A reference is enabling if it teaches those of ordinary skill in the art enough that they can carry out the invention without "undue experimentation." Elan Pharmaceuticals, lnc. v. Mayo Foundation, 346 F. 3d 1051, 057 (Fed. Cir. 2003).

Evans et a. do not enable a person of ordinary skill in the art to make the claimed isolated polypeptide for at least the following reasons. The anti-C5 antibody disclosed in Evans et al. was produced by animal immunization. (Col. 31, 1. 55-col 32, 1. 3.) Notable difficulty in raising antibodies against conserved proteins regions when taking a classical approach of an immunization of an animal with a peptide corresponding to the conserved region has been much appreciated. Mazari et al., "The cleavage site of C5 from man and animals as a common target for neutralizing human monoclonal antibodies: in vitro and in vivo studies," Eur. J. Immunol. (2002), 32:2773-2782 (Attached as Exhibit B), explain:

Antibodies... obtained by immunization are constrained by the limits of the immune system of the animal used for immunization. In particular, it tends to be very difficult to derive antibodies against conserved antigens by immunization. Mazari et al., p. 2778, col. 1.

Collet et al., "Evolution of mammalian apolipoprotein A-I and conservation of antigenicity: correlation with primary and secondary structure," J. Lipid Res. (1997), 38: 634-644 (Attached as Exhibit C), concur:
The natural selection that favors the conservation of functionally important proteins is a widely accepted idea in evolutionary theory. The antigenicity index of an important and invariant functional domain in protein is very low whereas the region outside the functional domain vary and can be highly antigenic. Collet et al., p. 639, col. 2.

Jemmerson et al., "Analysis of an evolutionary conserved antigenic site on mammalian cytochrome c using synthetic peptides," Proc. Natl. Acad. Sci. (1985), 82: 1508-15212, (Exhibit D) also note:
A commonly accepted view of the antigenicity of a protein is that the predominant epitopes correspond to those regions where the immunizing protein differs in amino acid sequence from the homologous protein of the immunized animal .... It should be noted, however, that reactivity to this region of cyt c may arise from circumstances that are consistent with the hypothesis that conserved regions of proteins are not, in general, immunogenic. Jemmerson et al., p. 1508, col. 1 and p. 1512, col. 1.

As evidenced by sequence alignments presented in Exhibit A, the epitope located at the cleavage site of C5 is highly conserved between different species (especially mouse and man). Therefore, introduction of the peptide corresponding to SEQ ID NO: 15 of Evans et al. into an animal (i.e., a mouse), is unlikely to result in a production of antibodies against this peptide. Stated otherwise, the disclosure of Evans et al. does not teach a person of ordinary skill in the art to obtain an antibody to an epitope with low immunogenicity without an undue experimentation, and is, thus, not enabling.

For the reasons stated above, Applicants acknowledge that Evans et al. does not expressly or inherently anticipate the claimed invention. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Applicant focuses on the 5G1.1 antibody taught by Evans et al. in order to support the assertion that Evans et al. does not teach an antibody that binds the cleavage site, which can inhibit the conversion of the C5 alpha chain to C5a and C5b and relies upon and the teachings of Mazari et al., Collet et al. and Jemmerson et al. to assert the lack of predictability of producing an antibody to the claimed peptide.

In contrast to applicant's assertions, Evans et al. clearly teach C5-specific antibodies, including human antibodies and antigen binding fragments thereof), wherein the antibodies should prevent the cleavage of C5 to form C5a and C5b (e.g., see column 20, paragraph 1) as well as targeting the cleavage site peptide (e.g., see column 21, paragraphs 2-4).

While Evans et al. does not explicitly teach the amino acid residues 727-744 of C5 per se, Evans et al. clearly teaches targeting the same or nearly the same cleavage site and corresponding properties of antibodies that inhibit the conversion or cleavage of C5, including the peptide spanning amino acids 725 through 754 of SEQ ID NO: 2 (the C5a cleavage site) (e.g., see column 21, paragraph 4).

Antibodies that bind the peptide spanning amino acids 725 through 754 of SEQ ID NO: 2 (the C5a cleavage site) that can prevent the cleavage of C5 to form C5a and C5b would have the inherent property of binding the claimed specificity of 727-744 of SEQ ID NO: 15, as both the prior art and the claimed invention are drawn to the same C5a cleavage peptide site specificity and the same functional properties.

Applicant's assertions, including the reliance upon the teachings of Mazari et al., Collet et al. and Jemmerson et al. have not been found convincing to detract from the clear teachings of the prior art to produce human antibodies to target the same or nearly the same cleavage site and corresponding properties of anti-C5 antibodies that inhibit the conversion or cleavage of C5, including the peptide spanning amino acids 725 through 754 of SEQ ID NO: 2.

Also, in contrast to applicant's assertions; disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. See In re Susi USPQ 423 (CCPA 1971). A known or obvious composition does not patentable simply because it has been described as somewhat inferior to some other product for the same use. See In re Gurley 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). See MPEP 2123.

Upon a review of the claims, it appears that claims 85-87 were inadvertently not included in the previous Office Action.
Given claims 85-87 are dependent on claim 37, these claims are subject to this rejection.

Given the breadth of competing and the antigen specificity of the prior art anti-C5 antibodies, claim 88 is included in this rejection.

The following of record is reiterated for applicant's convenience.

Evans et al. teach C5-specific antibodies, including human antibodies and antigen binding fragments thereof, including single chain antibodies (e.g., see Summary of the Invention and Description of the Preferred Embodiments), including human antibodies (e.g., column 21, paragraphs 5-7), classes of antibodies (see Antibody Engineering) as well as compositions (e.g., see Summary of the Invention) and articles of manufacture (e.g., kits) (e.g., see claims 6-9 on column 25), wherein the antibodies should prevent the cleavage of C5 to form C5a and C5b (e.g., see column 20, paragraph 1) as well as targeting the cleavage site peptide (e.g., see column 21, paragraphs 2-4), as well as the applicability of histidine tag sequences for purification (e.g., see column 24, paragraph 4) (see entire document)

Although Evans et al. does not explicitly teach the amino acid residues 731-740 of C5 per se, Evans et al. clearly teaches targeting the same or nearly the same cleavage site and corresponding properties of antibodies that inhibit the conversion or cleavage of C5.

Since the Office does not have a laboratory to test the reference antibody, it is Applicant's burden to show that the reference antibody does not bind or cross-react with the same cleavage site or epitope.
See In re Best, 195 USPQ 430, 433 (CCPA 1997); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); In re Fitzgerald, 205 USPQ 594 (CCPA 1980).

In the alternative, if the anti-C5 antibodies reduced to practice by Evans et al. do not necessarily bind or cross-react with the same targeted cleavage site / epitopes claimed encompassed in the instant invention,
one of ordinary skill in the art would have been motivated to make such cleavage site-specific antibodies, given the clear teachings of the prior art to target this specific region with the same functional properties of inhibiting C5 cleavage and inflammatory activities taught by Evans et al. and cited herein above.

A recitation of the intended use such as "for mycocardium damage" of the claimed invention (e.g., see claim 58) must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Given the various sources and classes of antibodies engineered for various utilities, one of ordinary skill in the art would have been motivated to provide antibodies of various forms, including chimeric antibodies of different species and classes to meet the needs of the particularly assays or utility as practiced and known at the time the invention was made and consistent with the teachings of the prior art.

Applicant's arguments have not been found persuasive.

10. Claims 37, 39-40, 56, 58, 72, 80-83 and 85-88 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Evans et al. (U.S. Patent 6,355,245) (892; of record) in view of Lonberg et al. (U.S. Patent No. 5,770,429) (892; of record).

Applicant's arguments, filed 10/06/2010, have been fully considered but have not been found convincing essentially for the reasons of record and that addressed above in the are rejected under 35 U.S.C. 102.

Applicant argues the following.

The Examiner has not met the burden of establishing a prima facie case of obviousness. Evans et al. alone, or in combination with Lonberg et al, do not teach or suggest all of the limitations of the claims. In particular, the cited references do not teach or suggest the antibody that recognizes a region corresponding to sequence 727-744 (SEQ ID NO: 15) of the C5 component of human complement, or a region having at least 80% homology thereto, wherein said antibody inhibits the conversion of the C5 alpha chain to C5a and C5b, as discussed in detail under the 102 rejection above.

The Examiner's rejection under 35 U.S.C. § 103(a) is based on the belief that the claimed antibody is inherently present in Evans et al., and that Applicants merely followed "the clear teachings of the prior art to target this specific region." (OA at p. 8.) Applicants respectfully assert that the Examiner's analysis is flawed, because the claimed antibody was not known earlier than the filing date of the claimed invention by Applicants. "Obviousness cannot be predicated on what is not known." In re Spormann, 363 F.2d 444, (C.C.P.A. 1966). Evans et al. do not disclose an antibody that recognizes specific region spanning amino acids 727-744 (SEQ ID NO:15). In fact, Evans et al. produce and describe an antibody that does not bind to the specified convertase cleavage cite. Therefore, Evans et al. alone is not sufficient to support a prima facie case of obviousness of the claimed invention, because it does not teach each and every element of the present claims.

Lonberg et al. do not cure the deficiencies of Evans et al. Lonberg merely teaches a method of production of humanized antibodies which is based on immunization of transgenic mice. Lonberg et al. do not teach or suggest production of an antibody that recognizes a region corresponding to sequence 727-744 (SEQ ID NO:15) of the C5 component of human complement or a region having at least 80% homology thereto, wherein said antibody inhibits the conversion of the C5 alpha chain to C5a and C5b. Therefore, combining Lonberg et al. with Evans et al. does nothing to cure the defects of Evans et al. and therefore reliance on this reference can not be used to establish a prima facie case of obviousness. Even assuming arguendo that the Examiner had established a prima facie case of obviousness (which Applicants do not concede), the unexpected superiority of Applicants' invention over the antibody of Evans et al. is sufficient to rebut the prima facie case of obviousness based on the disclosure of Evans et al., alone or in combination with Lonberg et al.

A determination of obviousness under 35 U.S.C. § 103 requires an evaluation of any evidence of secondary considerations such as unexpected results. Graham v. John Deere, 383 U.S. 1 (1966); MPEP 2141, p. 2100-113. Even when a claimed compound appears obvious on structural grounds, courts have long recognized "that unexpected properties can show that a claimed compound ... was not obvious when looked at as a whole." In re Mayne, 104 F.3d 1339, 1342 (Fed. Cir. 1997). "Evidence that a compound is unexpectedly superior in one of a spectrum of common properties.., can be enough to rebut a prima facie case of obviousness." In re Chupp, 816 F.2d 643, 646 (Fed. Cir. 1987) (emphasis added).

Applicants respectfully point out that the claimed anti-C5 antibody shows unexpectedly superior properties to anti-C5 antibody disclosed in Evans et al. In support of this contention, Applicants enclose as Exhibit B an article by Marzari et al. As stated in the article, the antibody taught in Evans et al. (which, as evident from Example 13 of Evans et aL, does not bind to the claimed epitope) "does not seem to be effective on C5 derived from other animals and this precludes its use in animal models, which would be helpful in the evaluation of their in vivo effects prior to use in man." (P. 2777, col. 1). Thus, this cross-reactivity of the claimed antibody is an unexpected and superior property over the Abs disclosed in Evans et al. In addition, Applicants contend that binding of the claimed antibody to a convertase cleavage site of C5 is in itself an unexpected result. An X-ray structure of human complement component C5 has recently been solved by Fredslund et al, "Structure of an influence of a tick complement inhibitor on human complement component 5," Nature lmmun. (2008), 9:753-760 (attached as Exhibit E). Analysis of the published coordinates reveals that the region corresponding to the convertase cleavage site (i.e., amino acids 727-744, SEQ ID NO: 15) is buried inside the protein and is not readily accessible for binding. For the Examiner's convenience, an image displaying the C5 structure is attached as Exhibit F. For clarity, convertase cleavage site is depicted on the center of the protein whereas only backbone is shown for the rest of the protein. Therefore, it is highly unexpected that the claimed antibody is able to bind to the region that corresponds to the convertase cleavage site of the intact protein.

Since there was no teaching or suggestion of all the claim limitations in Evans et al, alone or in combination with Longberg et al., a prima facie case of obviousness is not established. Furthermore, the claimed invention clearly possesses unexpected superior properties over previously known anti-C5. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Consistent with the arguments under 35 U.S.C. 102, applicant focuses on the 5G1.1 antibody taught by Evans et al. to teach that Evans et al. does not teach an antibody that binds the cleavage site, which can inhibit the conversion of the C5 alpha chain to C5a and C5b and relies upon and the teachings of Mazari et al., Collet et al., Jemmerson et al. and Freslund et al. to indicate the lack of predictability of producing an antibody to the claimed peptide as well as the lack of teaching of Lonberg et al. about anti-C5 antibodies.

With respect to the lack of teachings with respect to anti-C5 antibodies by Lonberg et al., one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller , 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

In contrast to applicant's assertions, Evans et al. clearly teach C5-specific antibodies, including human antibodies and antigen binding fragments thereof), wherein the antibodies should prevent the cleavage of C5 to form C5a and C5b (e.g., see column 20, paragraph 1) as well as targeting the cleavage site peptide (e.g., see column 21, paragraphs 2-4).

While Evans et al. does not explicitly teach the amino acid residues 727-744 of C5 per se, Evans et al. clearly teaches targeting the same or nearly the same cleavage site and corresponding properties of antibodies that inhibit the conversion or cleavage of C5, including the peptide spanning amino acids 725 through 754 of SEQ ID NO: 2 (the C5a cleavage site) (e.g., see column 21, paragraph 4).

Antibodies that bind the peptide spanning amino acids 725 through 754 of SEQ ID NO: 2 (the C5a cleavage site) that can prevent the cleavage of C5 to form C5a and C5b would have the intrinsic property of binding the claimed specificity of 727-744 of SEQ ID NO: 15, as both the prior art and the claimed invention are drawn to the same C5a cleavage peptide site specificity and the same functional properties.

Applicant's assertions, including the reliance upon the teachings of Mazari et al., Collet et al., Jemmerson et al. and Freslund et al. have not been found sufficiently convincing to detract from the clear teachings of the prior art to produce human antibodies to target the same or nearly the same cleavage site and corresponding properties of anti-C5 antibodies that inhibit the conversion or cleavage of C5, including the peptide spanning amino acids 725 through 754 of SEQ ID NO: 2.

Also, in contrast to applicant's assertions; disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. See In re Susi USPQ 423 (CCPA 1971). A known or obvious composition does not patentable simply because it has been described as somewhat inferior to some other product for the same use. See In re Gurley 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). See MPEP 2123

Upon a review of the claims, it appears that claims 85-87 were inadvertently not included in the previous Office Action.
Given claims 85-87 are dependent on claim 37, these claims are subject to this rejection.

Given the breadth of competing and the antigen specificity of the prior art anti-C5 antibodies, claim 88 is included in this rejection.

In contrast to applicant's assertions of unexpected results, the following is noted.

The rationale to support a conclusion that the claims would have been obvious is that all the claimed elements of producing human antibodies to target the same or nearly the same cleavage site and corresponding properties of anti-C5 antibodies that inhibit the conversion or cleavage of C5, including the peptide spanning amino acids 725 through 754 of SEQ ID NO: 2 were known in the prior art and one skilled in the art could have arrived at the claimed invention by using known methods of generating human antibodies to antigens of interest, including human antigens in order to target molecules of interest for various utilities (e.g., detection, treatment, purification) with no change in their respective functions and the combination would have yielded nothing more than predictable results of producing human inhibitory antibodies that bound the C5 cleavage site.

The rationale to support a conclusion that the claims would have been obvious is that a method of producing human antibodies to target the same or nearly the same cleavage site and corresponding properties of anti-C5 antibodies that inhibit the conversion or cleavage of C5, including the peptide spanning amino acids 725 through 754 of SEQ ID NO: 2. was made part of ordinary capabilities of one skilled in the art based upon the teachings of the prior art. One of ordinary skill in the art would have been capable of applying the known recombinant methods of producing human antibodies to antigens of interest, including human molecules in the detection, targeting and purification of such molecules and would have been predictable to one of ordinary skill in the art at the time the invention was made.

The rationale to support a conclusion that the claims would have been obvious is that a particular known technique of producing human antibodies to target the same or nearly the same cleavage site and corresponding properties of anti-C5 antibodies that inhibit the conversion or cleavage of C5, including the peptide spanning amino acids 725 through 754 of SEQ ID NO: 2. was recognized as part of the ordinary capabilities of one skilled in the art. One of ordinary skill in the art would have been capable of applying these known techniques to target a known molecule such as C5, including the C5a cleavage site that was ready for improvement and the results would have been predictable to one of ordinary skill in the art.

The rationale to support a conclusion that the claim would have been obvious is that a person of ordinary skill has good reason to pursue the known options of producinge human antibodies to target the same or nearly the same cleavage site and corresponding properties of anti-C5 antibodies that inhibit the conversion or cleavage of C5, including the peptide spanning amino acids 725 through 754 of SEQ ID NO: 2. within his or her technical grasp. This leads to the anticipated success of detecting, treating or purifying C5. It is likely the product not of innovation but of ordinary skill and common sense.

Since producing human antibodies to a human antigen of interest would have been predictable at the time of the invention, there would have been reasonable expectation of successful of producing human antibodies that target the same or nearly the same cleavage site and corresponding properties of anti-C5 antibodies that inhibit the conversion or cleavage of C5, including the peptide spanning amino acids 725 through 754 of SEQ ID NO: 2. The prior art had recognized the advantages of human antibodies that targeted human molecules for various utilities and relied upon the generating human antibodies to accomplish this goal. The claims were obvious because it would have been obvious to try producing human anti-C5 antibodies to detect, target and purify C5 with a reasonable expectation of success.

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdiqital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Given that the prior art goal was to target C5, particularly the C5a cleavage site, incorporating the production of known techniques to produce human antibodies to human antigens of interest would have been routine to the ordinary artisan at the time the invention was made and therefore obvious in designing human antibodies to C5, including the C5a cleavage site with improved half-life and desirable functions.

The following is reiterated for applicant's convenience.

Evans et al. teach C5-specific antibodies, including human antibodies and antigen binding fragments thereof, including single chain antibodies (e.g., see Summary of the Invention and Description of the Preferred Embodiments), including human antibodies (e.g., column 21, paragraphs 5-7), classes of antibodies (see Antibody Engineering) as well as compositions (e.g., see Summary of the Invention) and articles of manufacture (e.g., kits) (e.g., see claims 6-9 on column 25), wherein the antibodies should prevent the cleavage of C5 to form C5a and C5b (e.g., see column 20, paragraph 1) as well as targeting the cleavage site peptide (e.g., see column 21, paragraphs 2-4), as well as the applicability of histidine tag sequences for purification (e.g., see column 24, paragraph 4) (see entire document)

Although Evans et al. does not explicitly teach the amino acid residues 731-740 of C5 per se, Evans et al. clearly teaches targeting the same or nearly the same cleavage site and corresponding properties of antibodies that inhibit the conversion or cleavage of C5.

Lonberg et al. has been added to provide further evidence of the motivation and obviousness of producing human antibodies at the time the invention was made, as evidenced by the following.

"One of the major impediments facing the development of in vivo therapeutic and diagnostic applications for monoclonal antibodies in humans is the intrinsic immunogenicity of non-human immunoglobulins. For example, when immunocompetent human patients are administered therapeutic doses of rodent monoclonal antibodies, the patients produce antibodies against the rodent immunoglobulin sequences; these human anti-mouse antibodies (HAMA) neutralize the therapeutic antibodies and can cause acute toxicity. Hence, it is desirable to produce human immunoglobulins that are reactive with specific human antigens that are promising therapeutic and/or diagnostic targets. However, producing human immunoglobulins that bind specifically with human antigens is problematic" (see column 1, lines 54-67 in particular).

Lonberg et al. teach transgenic mice that, when immunized with an antigen, produce fully human [claims 3, 4] antibodies to that antigen (see entire document).

Given the teachings by Evans on antibodies that target and bind the C5 cleavage site and distinguishing the properties of other anti-C5 antibodies such as the 5G1.1 antibody that does not bind the C5a cleave site (e.g., see Example 13),
one of ordinary skill would have been motivated to generate anti-C5 antibodies that targeted the C5 cleavage site with anti-inflammatory properties.

Given the teachings of Evans et al. and Lonberg et al., it would have been obvious to one of ordinary skill in the art to make human antibodies with various constant regions for various detection, diagnostic and therapeutic utilities with humans, given the decreased immunogenicity and longer half-lives of human antibodies as well as providing the appropriate human immunoglobulin effector functions.

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Evans et al. and Lonberg et al. to obtain human anti-inflammatory anti-C5 antibodies that targeted the cleavage site of C5. According to Evans et al., a person of ordinary skill in the art would have been motivated to produce such resultant anti-inflammatory anti-C5 antibodies that targeted the cleavage site of C5 for various utilities a anti-inflammatory antibodies. From the teachings of the references, a person of ordinary skill in the art would have a reasonable expectation of success at the time the invention was made. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments have not been found persuasive.

11. Claims:

Claims 41-44, 46, 48 and 77-79 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 49 and dependent claims are deemed free of the prior art and would be allowable if rewritten to include the appropriate antigen specificity and function (e.g., see claim 37) in addressing the rejection under 35 U.S.C. 112, first paragraph, enablement above.

Claim 72 is allowable.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phillip Gambel/

Primary Examiner
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